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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MINXUE ZHENG, JOHN J. QUINN,
and BRIAN D. WARNER

Appeal 2009-007969
Application 10/667,191
Technology Center 1600

Decided: February 23, 2010

Before DONALD E. ADAMS, ERIC GRIMES, and
RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the rejections of claims 1-18 and 26-35. The Board's jurisdiction for this appeal is under 35 U.S.C. §§ 6(b) and 134. The rejections are reversed.

STATEMENT OF THE CASE

According to the Specification, intramolecular secondary structure may form in a single-stranded nucleic acid molecule when complementary nucleotide sequences within the molecule hybridize together (Spec. 1-2: ¶¶ 3-4). Such secondary structures can mask or conceal allelic variations associated with the regions of secondary structure (*id.* at 3: ¶ 8). As a result, a primer designed to detect a nucleotide variation may be unable to hybridize with the variation, producing no signal even when the variation is present (*id.* at 1-2: ¶¶ 3-5). To address this problem, the Specification describes a dual-purpose primer with a primer sequence and a blocking sequence. In certain embodiments, the primer is utilized to amplify a target sequence of interest (*id.* at 3: ¶ 9; 5: ¶ 19). After amplification, the blocking sequence hybridizes to its complement in the amplified sequence of interest, blocking unwanted secondary structure and revealing the masked allelic variation (*id.*).

Claims 1-18 and 26-35 are pending and stand rejected by the Examiner as follows:

1. Claims 1-18 and 26-35 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement (Ans. 3);

2. Claims 1-5, 9, 12-14, and 26 under 35 U.S.C. § 102(b) as anticipated by Wilton (Wilton et al., Snapback SSCP Analysis: Engineered Conformation Changes for the Rapid typing of Known Mutations, HUMAN MUTATION, vol. 11, pp. 252-258 (1998)) (Ans. 5);

3. Claims 1, 2, and 4-7 under 35 U.S.C. § 102(b) as anticipated by Bannwarth (Bannwarth et al., US 5,573,906, Nov. 12, 1996) (Ans. 7);

4. Claims 1 and 5-8 under 35 U.S.C. § 102(b) as anticipated by Laibinis (Laibinis et al., US 2002/0028455 A1, Mar. 7, 2002) (Ans. 9);

5. Claims 1, 17, and 18 under 35 U.S.C. § 102(b) as anticipated by Beattie (Beattie et al., US 6,268,147 B1, Jul. 31, 2001) (Ans. 10);

6. Claims 27-32 under 35 U.S.C. § 103(a) as obvious in view of Wilton and the Stratagene Catalog (Stratagene catalog, p. 39 (1988)) (Ans. 11).

7. Claim 28 under 35 U.S.C. § 103(a) as obvious in view of Bannwarth and the Stratagene catalog (Ans. 13).

8. Claims 28-34 under 35 U.S.C. § 103(a) as obvious in view of Beattie and the Stratagene catalog (Ans. 14).

9. Claims 10, 11, 15, and 16 under 35 U.S.C. § 103(a) as obvious in view of Wilton and Fisher (Fisher, US 6,054,568, Apr. 25, 2000) (Ans. 16).

Claim 1 is representative and reads as follows:

> 1. A dual-purpose primer for amplifying a target nucleotide sequence in a target molecule, wherein the target molecule has a secondary structure forming region and further wherein the target nucleotide sequence contains a site of interest proximal to or contained within the secondary structure forming region wherein the primer comprises: (a) a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region; and (b) a blocking sequence substantially complementary to a segment of the secondary structure forming region, wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest.

CLAIM INTERPRETATION

Statement of the Issue

Did the Examiner properly interpret the scope of claim 1 by ignoring its functional limitations?

Principles of Law

> A patent applicant is free to recite features of an apparatus either structurally or functionally. See *In re Swinehart*, 439 F.2d 210, 212, (CCPA 1971) ("[T]here is nothing intrinsically wrong with… [defining something by what it does rather than what it is] in drafting patent claims."). Yet, choosing to define an element functionally, i.e., by what it does, carries with it a risk. As our predecessor court stated in *Swinehart*, 439 F.2d at 213: where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on.

In re Schreiber, 128 F.3d 1473, 1478 (Fed. Cir. 1997).

Analysis

The functional limitations

Claim 1 is to a dual-purpose primer for amplifying a target nucleotide sequence in a target molecule. The dual-purpose primer comprises two key elements, recited in functional, rather than structural, terms. We address each below:

- "*(a) a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region*"

The dual-primer is recited to have a "primer sequence." The primer sequence is not described as having a specific structure or sequence. Instead, the primer is recited to have "a primer sequence complementary to a segment of the target nucleotide sequence." The term "primer" is defined in the Specification as "an oligonucleotide . . . which is capable of acting as a point of initiation of synthesis when placed under conditions in which synthesis of a primer extension product that is complementary to a nucleic acid strand is induced" (Spec. 8: ¶ 31). From its definition in the Specification, it would be understood that nucleotide sequence complementarity is necessary for the primer to serve as an initiator of nucleic acid synthesis. Thus, limitation (a) requires the "primer sequence" to be capable of acting as an initiator of nucleic acid synthesis. Any nucleotide sequence which is capable of this function would meet the claimed limitation; it is not limited to a particular sequence of nucleotides or size.

- "*(b) a blocking sequence substantially complementary to a segment of the secondary structure forming region, wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest.*"

Secondly, the dual-purpose primer is recited to have a "blocking sequence." The "blocking sequence" is not required by the claim to have a specific sequence of nucleotides. Rather, it is defined by the claim as complementary to a "secondary structure forming region" and to have the function of disrupting "formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of

interest." Therefore, to meet the "blocking sequence" limitation, a dual-purpose primer must comprise a portion which is complementary to a region that is capable of forming secondary structure *and* which disrupts the secondary structure when hybridized to the region.

The Examiner did not give weight to the "blocking sequence" limitation because it was a "functional limitation," arguing that "such functional limitations and recitations of intended use confer no structural limitations to the claimed primer" (Ans. 3).

The Examiner erred in interpreting the claim. "A patent applicant is free to recite features . . . either structurally or functionally." *In re Schreiber*, 128 F.3d at 1478. A claim element which is recited in terms of function, instead of structure, still limits the claim. (*Microprocessor Enhancement Corp. v. Texas Instruments Inc.*, 520 F.3d 1367, 1375 (Fed. Cir. 2008) ("Functional language may also be employed to limit the claims without using the mean-plus-function format.")) The patent statute specifically provides for a class of functional limitations written in "means-plus-function" format, where the claimed element is recited "as a means or step for performing a specified function without the recital of structure, material or actions." 35 U.S.C. § 112, sixth paragraph. Thus, claiming "blocking sequence" in terms of its function, rather than structure, was not a proper basis to disregard it as a limitation of the claim.

The "dual-purpose primer"

According to the Specification, the primer is characterized as a "dual-purpose" because it has both a "primer sequence," which is effective to amplify a target nucleic acid, and a "blocking sequence," which disrupts

secondary structure in a single-stranded form of the target nucleic acid (Spec. 3: ¶ 8). These two sequences correspond to elements (a) and (b), respectively, of claim 1.

The "primer" portion (element "(a)") of the dual-purpose primer "is relatively short, generally on the order of 10 to 30 bases in length" and the blocking sequence portion (element "(b)") "can also be relatively short," for example, 8 to 12 bases in length (*id.* at 14: ¶ 57). Dual-purpose primers from 55 to 59 nucleotides were utilized in Example 2 (*id.* at 26-27: ¶ 98; SEQ ID NOS: 16-23). However, we do not limit the dual-purpose primer to these sizes; rather, any sized nucleic acid which can perform the primer and blocking sequence functions would meet the limitations of the claim.

WRITTEN DESCRIPTION REJECTION

Claims 1-18 and 26-35 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement (Ans. 3).

Statement of the Issue

Did the Examiner err in rejecting claim 1 for failing to comply with the written description requirement?

Principles of Law

A fully described genus must allow one skilled in the art to "visualize or recognize the identity of the members of the genus" and to "distinguish the claimed genus from others." *University of California v. Eli Lilly & Co.* ("*Lilly*"), 119 F.3d 1559, 1568 (Fed. Cir. 1997).

"[A]pplicants have some flexibility in the 'mode selected for compliance' with the written description requirement," but a specification

must "set forth enough detail to allow a person of ordinary skill in the art . . . to recognize that the inventor invented what is claimed." *University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 928 (Fed. Cir. 2004).

> [T]he written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 964 (Fed. Cir. 2002) (emphasis omitted, alterations in original).

"[W]hat is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue." *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005). "[I]t is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. *See In re Angstadt*, 537 F.2d 498, 504 (CCPA 1976)." *Capon*, 418 F.3d at 1359.

Analysis

Citing *Fiers v. Revel,* 984 F.2d 1164 (Fed. Cir. 1993), *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 927 F.2d 1200 (Fed. Cir. 1991), and *University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997), the Examiner determined that the Specification did not fully describe the genus of the claimed nucleic acids because the "skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acids" (Ans. 4). The

Examiner found that the claims encompassed "any polynucleotide for which a target sequence exists *or could be synthesized*," but determined that the Specification did not describe a representative number within the scope of the claim (*id.* at 5).

> Since no specific polynucleotide sequence or no specific template sequence is recited, Applicants have not described the sequence information required to define the genus of all primers that would provide the requisite functional limitations required by the claims.
>
> Therefore, . . . Applicants have not adequately defined the genus in terms of the structure required to perform the function and have not adequately described the enormous number of potential primers falling within the genus claimed.

(*Id.*)

In the *Fiers*, *Amgen*, and *Eli Lilly* cases, the inventor asserted to have invented a nucleic acid molecule coding for a specific polypeptide. Because the novelty of the sequence, itself, was at issue, the court imposed the requirement under section 112, first paragraph, that the Specification describe the complete nucleotide sequence of the claimed nucleic acid, along with a representative number of examples within the scope of the claim. However, this was not an inflexible requirement for all nucleic acid claims. As discussed in *Capon*, support for a generic claim "to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue." *Capon*, 418 F.3d at 1359.

In this case, the inventors do not assert to have invented a specific nucleotide sequence. Rather, the invention is characterized as a conventional primer sequence coupled to a blocking sequence, where the

latter unmasks allelic variations that are otherwise concealed by secondary structure when the dual-purpose primer is used in amplification reactions (Spec. 4: ¶ 13, 5: ¶ 19, 18: ¶ 69; & 19: ¶ 72). As indicated in the Specification, selection of suitable sequences with these functions for any given target sequence would have been routine (*id.*). It was not appropriate to require a written description of a representative nucleic acid as in the line of cases represented by the *Lilly* case because the invention is not a specific nucleic acid sequence, per se, but a generic dual-purpose primer with priming and blocking functions to enable detection of masked allelic variations.

There is no rigid test for compliance with the written description requirement. Rather, the Specification must set forth sufficient detail to establish that the inventors invented what is claimed. Written description of a complete invention can be shown by sufficiently detailed and identifying characteristics. *Enzo*, 323 F.3d at 964. The written description must be viewed in the eyes of the ordinary skilled worker and the knowledge accorded to him. *See Capon*, 418 F.3d at 1359. To this end, the Specification established that the existing knowledge in the art was substantial: primer design, hybridization, and secondary structure were well characterized at the time of the invention (Spec. 1-2; 2: ¶ 6; 9: ¶ 36). Using this knowledge, persons of ordinary skill in the art could routinely select dual-purpose primers with priming and blocking functions. The Specification generically described the dual-purpose primer (*id.* at 5: ¶ 19; 13: ¶ 53; 14: ¶ 57; 17: ¶ 67; 18: ¶¶ 68-69). Based on the generic description coupled with the established maturity of the field, persons of ordinary skill

in the art would have recognized that the description of the invention was complete.

ANTICIPATION REJECTIONS

Claims 1-5, 9, 12-14, and 26 stand rejected under 35 U.S.C. § 102(b) as anticipated by Wilton (Ans. 5).

Claims 1, 2, and 4-7 stand rejected under 35 U.S.C. § 102(b) as anticipated by Bannwarth (Ans. 7).

Claims 1 and 5-8 stand rejected under 35 U.S.C. § 102(b) as anticipated by Laibinis (Ans. 9).

Claims 1, 17, and 18 stand rejected under 35 U.S.C. § 102(b) as anticipated by Beattie (Ans. 10).

Statement of the Issue

Do the Wilton, Bannwarth, Laibinis, and Beattie publications describe the claimed dual purpose primer with primer and blocking sequences?

Principles of Law

"To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." *In re Schreiber*, 128 F.3d at 1477.

The PTO does not have the ability "to manufacture products or to obtain and compare prior art products." *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977). Thus, once "the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990).

Analysis

The Examiner had the burden of establishing a sound basis to believe that claimed dual-purpose primer was described in the prior art. This burden was not met. Although the Examiner provided evidence that the prior art nucleic acids of Wilton, Bannwarth, Laibinis, and Beattie, each had a sequence capable of performing the primer function of element (a), the Examiner improperly gave element (b) no weight. The Examiner asserted that the "blocking sequence" imparted no limitation to the claim and did not compare it to the prior art (Ans. 6, 8, 9, and 11). As discussed above, a claim element which is recited in terms of function, instead of structure, still limits the claim. The Examiner therefore erred in interpreting claim 1 by disregarding an explicit limitation of the claim. As the Examiner did not provide a factual basis upon which to believe that the primers of Wilton, Bannwarth, Laibinis, and Beattie comprise a "blocking sequence" capable of disrupting secondary structure, we are compelled to reverse all the rejections for anticipation.

OBVIOUSNESS REJECTIONS

Claims 27-32 stand rejected under 35 U.S.C. § 103(a) as obvious in view of Wilton and the Stratagene Catalog (Ans. 11).

Claim 28 stands rejected under 35 U.S.C. § 103(a) as obvious in view of Bannwarth and the Stratagene Catalog (Ans. 13).

Claims 28-34 stand rejected under 35 U.S.C. § 103(a) as obvious in view of Beattie and the Stratagene Catalog (Ans. 14).

Claims 10, 11, 15, and 16 stand rejected under 35 U.S.C. § 103(a) as obvious in view of Wilton and Fisher (Ans. 16).

All the claims rejected under § 103(a) require a dual-primer with (a) a primer sequence and (b) a blocking sequence. As the Examiner did not establish that the cited prior art publications described the claimed blocking sequence, we are compelled to reverse the rejections.

REVERSED

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